or more of vaginal secretions, intestinal secretions, respiratory secretions and feces, capable of neutralizing said pathogenic organism.

Remarks

Procedural Matters

As a result of a restriction requirement election, Applicants have cancelled Claim 25 and Claims 1-18, which are directed to non-elected subject matter. Please note that Applicants reserve the right to file subsequent patent application encompassing these Claims and their cancellation should not be construed as an abandonment of the subject matter. Claims 19-24 and 26-32 remain pending in the present application.

In the documents filed herewith, Applicants are complying with the sequence listing requirements under 37 CFR §1.821-1.825. In addition, Applicants have inserted the appropriate sequence identifier information in the Specification and the Claims as indicated by the above amendments.

The undersigned hereby states that the computer readable form copy (CRF copy) of the Sequence Listing and the paper copy of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.825(a) and (b), respectively, are the same and contain no new matter. Accordingly, entry of the Sequence Listing into the above-captioned case is respectfully requested.

Applicants also have inserted priority patent application information into the Specification, as requested, and have filed herewith the formal drawings (5 sheets) for this application.

Claims 19-32 were objected to, and were rejected under 35 USC §112, second paragraph, for including reference to limitations set forth in a non-elected claims. Through the above amendments, Applicants have incorporated claim language from the non-elected claims, as appropriate, into the pending claims, to overcome the objection to Claims 19-32. In addition, Applicants' amendment of the claims overcomes the rejections under 35 USC §112, second paragraph, because the claims now properly incorporate the necessary claim language to remove the antecedent basis rejections.

Applicants believe that their actions should successfully resolve all outstanding procedural issues and respectfully request that all objections and §112, second paragraph, rejections should be withdrawn.

Please note that in the amended claims, Applicants have replaced the word "lung" with "respiratory" and have inserted the phrase "viral or bacterial" to describe the antigen. Support for the amended claims is found in Claims 1, 7, and 16, as well as page 7, lines 10-15 of the Specification. Therefore, Applicants believe that no new matter is described.

Rejection under 35 USC 102

Claims 19-21 and 26-32 have been rejected under 35 USC 102(e) as being anticipated by US Patent 5,726,292 ("Lowell"). Applicants respectfully traverse. The present claims are directed to processes for inducing *neutralizing* mucosal antibodies; which is unlike the Lowell reference. Although the Lowell reference describes antibodies that recognize an antigen, they are not neutralizing antibodies. For example, if the antibody binds to an epitope that is located in a non-critical site of the antigen or a site on the antigen which, when present in the pathogen, is not accessible to the antibody, the antibody will not be neutralizing. Neutralizing antibodies are those that interfere with, or impede, a deleterious or undesired function of the microorganism. Therefore, a neutralizing antibody performs differently than other antibodies. For these reasons, Applicants assert that the Lowell reference does not anticipate the stated claims.

Furthermore, the antibodies produced in the Lowell reference (Columns 18-20) are directed toward serum antibodies rather than mucosal antibodies as claimed, or the antibodies were produced without the use of a hydrophobic sequence as claimed, or the antibodies were raised against non-viral or non-bacterial antigens or peptides. Moreover, in those instances in which the Lowell conjugates conferred protection against a subsequent challenge, the protection was against a systemic challenge resulting in high levels of serum antibodies. Applicants respectfully request withdrawal of the 35 U.S.C. 102(e) rejection in view of these remarks.

Rejection under 35 USC 103(a)

Claims 22-26 have been rejected under 365 USC 103(a) as being obvious over Lowell in view of VanCott, T.C., *et al.*, "Characterization of a soluble, oligomeric HIV-1 gp160 protein as

a potential immunogen", J. Immunol. Methods, 183:103-117 (1995) ("VanCott"). Applicants respectfully traverse.

The VanCott reference does not remedy the deficiencies of the Lowell reference, which is discussed above. Although VanCott provides an assessment of the oligomeric structure and antigenic properties of purified gp160 protein, it describes serum antibodies only. Therefore, it does not discuss how to generate the claimed neutralized mucosal antibodies, nor does the VanCott reference utilize a proteosome complex or nanoemulsion. [See pages 5-6 of the present specification for a further description of the VanCott reference.]

It is respectfully requested that the obviousness rejection be withdrawn.

Applicants believe the application is now in condition for allowance. If the Examiner believes it would be helpful to discuss the application, please call the undersigned, Karen Dow, at (858) 720-7960, or send a facsimile to (858) 720-5125.

Attached hereto is a marked-up version of the changes made to claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing Docket No. 406462000200. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: December 21, 2001 By: Karen Babyak Dow

Karen B. Dow
Registration No. 29,684
Morrison & Foerster LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130-2332
Telephone: (858) 720-7960
Facsimile: (858) 720-5125

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at page 8, line 4, has been amended as follows:

The endogenous hydrophobic sequence or the exogenous hydrophobic sequence is an amino acid sequence is preferably between about 5 and about 29 residues. Preferred short exogenous hydrophobic sequences are Phe-Leu-Leu-Ala-Val (SEQ ID NO:2) or Val-Ala-Leu-Leu-Phe (SEQ ID NO:3). The exogenous hydrophobic material may also be C8-C18 fatty acyl group, preferably lauroyl.

Paragraph beginning at page 26, line 3, has been amended as follows:

The results of several tests of the production and use of the present vaccine composition are detailed in TABLES 2-4. All vaccines were prepared as described below. Briefly, the peptides, with or wthout added cysteines, were synthesized by standard solid phase technology. While still on the resin, a lauroyl group was added to the amino terminus as described below or the pentapeptide hydrophobic foot, Phe-Leu-Leu-Ala-Val (FLLAV) (SEQ ID NO:2), was added by simply continuing the synthesis. Except when noted otherwise, all vaccines were prepared by dissolving the peptides and/or the proteosomes in TEEN-1% detergent buffer and then exhaustively dialyzing away the detergent.

Paragraph beginning at page 31, line 9, has been amended as follows:

The synthetic DNA hydrophobic decapeptide anchor sequence (1 μg) identified below was then added and ligated to the SmaI/SalI cut pR32 (100ηg) in 30 μl ligase buffer with one unit of T4-DNA ligase at 4°C for 16 hours. The hydrophobic decapeptide coding sequence was:

5' GGT GGT TAC TGC TTC GTT GCT CTG CTG TTC TGA G (SEQ ID NO:17)

3'CCA CCA ATG ACG AAG CAA CGA GAC GAC AAG ACT CAGCT (SEQ ID NO:18).

In the Claims:

19. (Amended) A process for inducing a neutralizing antibody response in a subject against a pathogenic organism resulting in neutralizing antibodies in one or more of vaginal secretions, intestinal secretions, [lung] respiratory secretions and feces, which process comprises

administering to the subject an effective amount of a vaccine composition [according to claim 1] capable of eliciting neutralizing antibodies in a subject to a pathogenic organism which antibodies are present in vaginal secretions, intestinal secretions, respiratory secretions or feces, which composition comprises:

(a) a viral or bacterial antigen comprising a protein having

(i) an endogenous hydrophobic sequence of between about 3 and about 50 non-polar or uncharged amino acids;

(ii) added to the protein, an exogenous hydrophobic material comprising a sequence of between about 3 and about 50 non-polar or uncharged amino acids or a C8-C18 fatty acyl group; or

(iii) both (i) and (ii),

(b) complexed with said antigen, a composition comprising proteosomes, bioadhesive nanoemulsions, or both,

wherein said complexed or coupled protein maintains a native structure of antigenic epitopes such that, upon administration to said subject, the antigen induces neutralizing antibodies in one or more of vaginal secretions, intestinal secretions, respiratory secretions and feces, capable of neutralizing said pathogenic organism.

21. (Amended) A process according to claim 19 wherein the exogenous hydrophobic material of said vaccine composition is lauroyl, Phe Leu Leu Ala Val (SEQ ID NO:2) or Val Ala Leu Leu Phe (SEQ ID NO:3).

26. (Amended) A process according to claim 19 wherein the protein [or peptide] is recombinantly produced.

27. (Amended) A process according to claim 19, wherein said vaccine composition is formed by

(a) bonding the hydrophobic material to said protein [or peptide] to form a hydrophobic-hydrophilic compound; and

(b) admixing said compound with said proteosomes, bioadhesive nanoemulsions, or both such that said antigen is complexed with said proteosomes or nanoemulsion.

30. (Amended) A process for inducing a neutralizing antibody response in a subject against a pathogenic organism resulting in neutralizing antibodies in one or more of vaginal secretions, intestinal secretions, [lung] respiratory secretions and feces, which process comprises administering to said subject by intranasal or respiratory route a vaccine composition [according to claim 16] formulated for intranasal or respiratory administration and capable of eliciting neutralizing antibodies in a subject to a pathogenic organism which antibodies are present in vaginal secretions, intestinal secretions, respiratory secretions or feces, which composition comprises:

(a) a viral or bacterial antigen comprising a protein having

(i) an endogenous hydrophobic sequence of between about 3 and about 50 non-polar or uncharged amino acids;

(ii) added to the protein, an exogenous hydrophobic material comprising a sequence of between about 3 and about 50 non-polar or uncharged amino acids or a C8-C18 fatty acyl group; or

(iii) both (i) and (ii),

(b) complexed with said antigen, a composition comprising proteosomes, bioadhesive nanoemulsions, or both,

wherein said complexed or coupled protein maintains a native structure of antigenic epitopes such that, upon administration to said subject, the antigen induces neutralizing antibodies in one or more of vaginal secretions, intestinal secretions, respiratory secretions and feces, capable of neutralizing said pathogenic organism.